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Comparison of Data On Scientometric Analysis Of The Articles on Six Hereditary Disorders Published Up To 1990 And During 1991-2014 Seen In India.

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Abstract
The present paper uses some scientometric indicators to examine the research output on six hereditary disorders (Down syndrome, Sickle cell anemia, G6PD deficiency, Hemophilia A, Hemophilia B, von Willebrand disease) seen in India. The articles published on these disorders wereretrieved from PUBMED database. The raw data was systematically arranged in MS-Excel sheets and then analyzed. Totally 1,606 articles published from India on the above mentioned disorders were extracted from the database. The articles published up to 2014 were extracted.
The range of time period was between 60-70 years. After deleting incomplete or non-specific entries 1,175 articles were available for further analysis. This data is divided into two time blocks viz. up to 1990 and during 1991-2014 and was compared. Scientometric indicators like journal-wise analysis, year-wise analysis, identification of top five most prominent journals for each time block and most productive years for each disorder were used to analyse this data.

Keywords – scientometric analysis, hereditary disorders, molecular biology

Introduction
Research plays an important role in increasing the knowledge of a scientist. Evaluating scientific productivity of a particular topic or subject is very useful to the researcher who is working in that area.
Scientometrics is defined as the quantitative study of scientific literature. This analysis is done to evaluate the growth of the particular subject. This is useful to policy makers, funding agencies in addition to research scholars. Several indicators like year-wise or journal-wise trend of publications, identifying most productive year of publications or most prominent journals where maximum numbers of articles are published, are used for this purpose.
Hereditary disorders are a group of disorders in which defective genes are transmitted from parents to children even though parents themselves do not suffer due to them. In such cases parents are called ‘carriers’. Two ‘carrier’ parents may transmit the defective genes to a child where the disease will be developed. These disorders cannot be cured by medicines. Currently prevention of these disorders by prenatal diagnosis is the only solution. Several hereditary disorders are seen in our country. Sickle cell anemia, Hemophilia A, Hemophilia B, von Willebrand disease, Down syndrome, G6PD Deficiency are some of the common hereditary blood disorders seen in our country.

Sickle cell anemia is an inherited group of disorders that affects production of normal hemoglobin molecule People with this disorder produce atypical hemoglobin molecule called hemoglobin S (Sickle hemoglobin). This is formed due to a mutation in the beta chain of haemoglobin molecule, the gene for which is located on chromosome 11. Sickle hemoglobin molecules stick to one another and form long rod like structures which are responsible for making RBCs stiff, rigid and ultimately they assume sickle or crescent shape. Such RBC’s pile up and

causes blockages and damages various organs in the body. These RBC's also die early in their body causing anemia. Blockages are responsible for pain. It is mainly seen in Africa, India (mainly among tribal population) and the Arabian Peninsula.

HemophiliaA is caused by mutation or change in one of the genes that provides instructions for making the clotting factor proteins which is required to form a blood clot. This disorder is inherited as an 'X' linked recessive pattern. Therefore usually males are affected while females are carriers. In this disorder there is a deficiency in clotting factor VIII protein which results in increased bleeding. Individuals generally suffer due to internal and external bleeding episodes. It's prevalence in India is about 4 per 1, 00,000 individuals or 1 out of 10,000 male births.

Hemophilia B is also an inherited coagulation disorder. It is formed due to deficiency of factor IX. Like hemophiliaA it is also inherited as an X linked recessive pattern. The common symptoms include easy bruising and bleeding. In this disorder periodontal disease and bleeding is high. This disorder is less common than HemophiliaA . It's prevalence in India is 0. 1 per 1,00,000 individuals or 1 out of 30,000 male births.

vonWillebrand disease is named after the Finnish physician Eric Adolf von Willebrand who first detected this condition in a small girl in 1924. It is the most common hereditary blood clotting disorder seen in humans. It is inherited in an autosomal dominant fashion. It is caused due to deficiency in quality or quantity of vWF which is required for platelet attachment. It occurs among males and females equally. The symptoms include varying degrees of bleeding tendency which are in the form of nose bleeds, bleeding of gums while among females heavy menstrual periods and heavy blood loss during delivery. Its prevalence is about 1% of the general population in India.

Down syndrome is a condition in which a person has an extra chromosome which is formed by a random error during the formation of eggs and sperms. This chromosome comes from chromosome 21. Therefore this is also called 'Trisomy 21'. It is named after Dr. John Down, the British doctor who fully described the syndrome in 1866. Thisdisease can be detected by chromosome analysis on a blood or skin sample. The main symptoms include distinct facial appearance, poor muscle tone, intellectual disability and developmental delay since infancy. It occurs in about 1 per 1000 babies born every year. About 23000 to 25000 babies are born in India every year with this disorder which is the highest rate in the world. The average IQ of these children is about 50.

Glucose 6 Phosphate Dehydrogenase (G6PD) deficiency is an inborn error of metabolism. The deficiency of the enzyme G6PD causes red blood cells to breakdown prematurely which is called hemolysis. This causes anemia. It is an X linked disorder inherited in a recessive pattern. Therefore, generally males are affected and females are carriers. Most of the time the affected males have no symptoms. However, certain specific triggers like stress due to infections, certain medications like anti material drugs like quinine, primaquineetc., ingestion of foods like Fava Beans may develop systems of intravascular hemolysis like dark urine, shortness of breath, jaundice, renal failure and in some cases even death. It is commonly seen in Africa, Asia the Mediterranean and the Middle East.

Review of literature

Several studies have reported analysis of literature published on various disorders seen in India. This include Alzheimer's disease (Gupta and Bala 2013), Autism (Jeyshankar and Velaichamy 2016), Leprosy (Rajeshwari et al 2014), HIV/AIDS (Gupta et al 2011), Dengue (Gupta et al 2014), etc.

When the literature on the above mentioned six hereditary disorders was searched; only four articles where scientometric analyses on research output on some of the disorders selected in the present study has been done. Gupta (2012) analysed the research output on five hereditary disorders viz. sickle cell anemia, von Willebrand disease, thalassemia, haemophilia (combined both A and B) and thrombopenia. Second article was on haemophilia research. Vellaichamy and Jeyshankar (2018) evaluated the growth in publications on haemophilia (combined both A and B) research output

published during 2003-2017. Gupta and Gupta (2018) analysed 436 articles on Sickle cell anemia published during 2008-2017 from India.They found an annual average growth rate of 9.97% during this time period. Global publication share of India was 3.8%. The cumulative growth of Indian publications increased from 168 to 268 publications from 2008-2012 to 2013-2017 showing a growth rate of 59.52% which is very significant.The fourth article was by Okoroiwu et al (2020) who recently analysed global sickle cell disease research from 1997-2017 aand concluded that although the growth of scientific literature in Sickle cell disease was high, still there is enough room to conduct research on this disease covering areas like treatment,genetherapy,anti-sickling agents, allogeneic hematopoietic stem cell transplant etc.

So in the present paperauthors attempted extensive preliminary analysis of the articles published on above mentioned six hereditary disorders seen in India.

Objectives

1. To examine the year-wise trend of publications on the above mentioned six Hereditary disorders.
2. To examine journal-wise trend of publications.
3. To identify most productive years of publications in the case of each disorder.
4. To identify most prominent journals for each disorder where maximum number of articles are published over the specific time.

Scope and limitations of the study

The present study would help the scientists who are working on these disorders. They will get up to date information about the pattern of publications on these disorders. This study would help them to design the new projects to fill up the gaps in various areas. This would also help the policy makers and funding agencies during funding of the projects. Such type of extensive scientometric analysis on these disorders has not been done earlier. Therefore the major limitation was getting the published literature on these disorders for comparison. This study is limited up to analysis of published articles on six hereditary disorders from India up to 2014.

Data source

Various database like INDMED, SCIENCE DIRECT, SCOPUS and PUBMED were considered for retrieval of publications. Out of these, PUBMED database was selected as it is a comprehensive and free database and also contains very old articles.

Methodology

Specific strings or keywords were used to extract the data on each disorder from PUBMED database. Following strings were used to extract the data pm each hereditary disorders.

1) Sickle cell anemia - Sickle cell anemia, Sickle cell disease, Sickle hemoglobin.
2) Hemophilia A - Hemophilia A, Factor VIII.
3) Hemophilia B - Hemophilia B, Christmas disease, Factor IX.
4) von Willebrand disease - vonWillebrand disease, vWD, von Willebrand Factor, vWF.
5) Down syndrome - Down syndrome, Trisomy 21, Aneuploidy.
6) G6PD deficiency - G6PD deficiency, Fava beans.

Thus publications on these disorders published up to 2014 were retrieved. For geographical segregation, an additional string ‘India’ was added to each file. This helped to get the articles published from India on each disorder. Articles on each disorder were considered from the year when the first article on that disorder was listed in PUBMED database. Therefore the time coverage for each disorder was different and ranged between 60-70 years. For further analysis, data from each file was separated into two groups. Articles published up to 1990 and articles published during 1991-2014. In this paper analysis of data published up to 1990 and during 1991-2014 from India on each disorder is compared.

While scrutinizing the files, it was found that there were many annotation errors especially in old publications. These included absence of PMID number, absence of proper title etc. All these incomplete entries were deleted. Apart from this, it was also observed that many nonspecific publications not related to the particular disorder were also listed under that disorder. For example, an article with the word 'Down' or 'Syndrome' in its title but not related to Down syndrome was listed under this disorder. Similarly articles related to hemolytic anemia due to various cancers were listed under G6PD deficiency. All such nonspecific entries were deleted from each file before analysis.

Data analysis

Details of the preliminary data retrieved from PUBMED database is shown in**Table1**.
Totally 1,606 articles published on six hereditary disorders from India were found while 93,919 articles published from all over the world on these disorders were found. After deleting entries due to annotation errors; this number reduced to 86,555. India's share in publication of articles on six disorders is 1.71% as compared to the world publications, while on individual disorders it varied between 1.01% - 3.39% as compared to world publications output data.
Table2 reveals number of articles under each disorder from India available for analysis after deleting annotation errors and nonspecific articles. 276 articles published on six disorders up to1990 were available for further analysis. While 899 articles published during 1991-2014 were available for analysis. Thus totally 1,175 articles published from India up to 2014 were analyzed.
Table 3 reveals year-wise trend of publications of articles published up to 1990 from India. Articles published on coagulation disorders viz. Hemophilia A, Hemophilia B and von Willebrand disease were very small as compared to those published on remaining three disorders. Most productive year for Sickle cell anemia was 1987 while that for G6PD deficiency and Down syndrome was 1990.
Table 4 depicts year-wise trend of publications of the articles published during 1991-2014 from India on six disorders. Comparatively more number of articles was published during this time block as compared to these published up to 1990. Most productive years are different for different disorders. They are 2012 for Sickle cell anemia, 2007 and 2014 for Hemophilia A, 2001 for Hemophilia B, 2005 for von Willebrand disease, 1992 for G6PD deficiency and 2013 for Down syndrome. G6PD deficiency shows a decreasing trend. Half-life for these disorders varies between 13-19 years. This clearly shows that speed of publications increased considerably during last 6-7 years of time block.
Figure 1 depicts journal-wise trend of articles published up to 1990 from India. In the case of G6PD deficiency 117 articles were published in 37 journals while in case of Sickle cell anemia 101 articles were published in 32 journals. In the case coagulation disorders (Hep A, Hep B and vWD) 6-13 articles were published in 2-5 journals
Figure 2 demonstrates journal-wise trend of articles published during 1991-2014. In the case of coagulation disorders number of articles published on each disorder and number of journals in which they were published, has increased considerably.
Table 5 reveals list of top five journals for each disorder where maximum number of articles were published up to 1990. Except for Down syndrome, the top journal for rest of the disorders was JAPI. Articles published in top five journals ranged between 6-58. Percent representation of articles published in top five journals varies between 48.72-100%
Table 6 shows list of top five journals for each disorder where maximum numbers of articles were published during 1991-2014. JAPI, Hemophilia, Indian Journal of Pediatrics and Annals of Hematology were the most prominent journals. Articles published in top five journals ranged between 25-91. In the case of coagulation disorders the articles published in top five journals ranged between 39.68-43.33%.

Table 1: Details of preliminary retrieval of data from PUBMED database on six genetic disorders published from India as well as from all over the world

Sr. No.	Disease	Country	PubMed Record
1	Down syndrome	India	430 (1.36)
	Down syndrome	Worldwide	31,548
2	G6PD deficiency	India	252 (3.39)
	G6PD deficiency	Worldwide	7,424
3	Hemophilia A	India	249 (1.29)
	Hemophilia A	Worldwide	19,312
4	Hemophilia B	India	83 (1.89)
	Hemophilia B	Worldwide	4,391
5	von Willebrand disease	India	75 (1.01)
	von Willebrand disease	Worldwide	7,435
6	Sickle cell aanemia	India	517 (2.17)
	Sickle cell anemia	Worldwide	23,809
TOTAL		**India**	**1,606 (1.17)**
TOTAL		**Worldwide**	**93,919***

Figures in brackets indicate percentage values

*After deleting the entries showing annotation errors like absence of PMID number, absence of proper titles and also deleting the lines showing headings like only author name, journal name, etc., this number is reduced to 86,555 for further analysis.
PMID number were also deleted. Then the total number of international publications reduced to 86,555.

Table 2: Number of articles published from India on six genetic disorders and available for analysis after deleting nonspecific publications

Genetic Disease	Up to 1990		1991-2014		Pub Med Records	After Non specific Deletions
	Pub Med Record	After non specific Deletions	Pub Med Record	After non specific Deletions		
Down syndrome	88	32	342	192	430	224
G6PD deficiency	124	117	128	118	252	235
Haemophilia A	19	13	230	210	249	223
Haemophilia B	07	06	76	73	83	79
vonWillebrand disease	10	07	65	63	75	70
Sickle cell anemia	174	101	343	243	517	344
Total	**422**	**276**	**1,184**	**899**	**1,606**	**1,175**

Explanation - 1,175 articles published from India were available for detail analysis.

Table 3: Year- wise publications of articles up to 1990 published from India on six genetic disorders.

Year	Sickle cell anemia	Hemophilia 'A'	Hemophilia 'B'	von Willibrand disease	G6PD deficiency	Down syndrome
1952	2	0	0	0	0	0
1953	0	0	0	0	0	0
1954	0	0	0	0	0	0
1955	0	0	0	0	0	0
1956	0	0	0	0	0	0
1957	0	0	0	0	0	0
1958	3	0	0	0	0	0
1959	0	0	0	0	0	0
1960	0	0	0	0	0	0
1961	0	0	0	0	0	0
1962	0	1	0	0	0	0
1963	1	0	0	1	2	0
1964	1	0	0	0	1	1
1965	0	0	0	1	0	1
1966	1	0	0	1	2	0
1967	3	0	0	0	4	0
1968	4	0	0	0	7	1
1969	6	0	0	0	3	0
1970	2	0	0	0	0	1
1971	1	0	0	0	6	1
1972	0	1	2	1	6	1
1973	4	0	1	1	5	2
1974	2	0	0	0	5	0
1975	3	0	0	0	3	2
1976	2	0	0	1	4	1
1977	3	0	0	0	6	1
1978	3	0	0	0	6	0
1979	3	0	0	0	1	1
1980	3	0	0	0	3	0
1981	5	2	1	1	7	4
1982	3	1	1	0	7	0
1983	4	0	0	0	4	1
1984	3	0	0	0	6	0
1985	3	0	0	0	7	1
1986	7	1	0	0	0	1
1987	10	2	0	0	5	3
1988	9	0	0	0	3	1
1989	4	0	0	0	5	2
1990	6	5	1	0	9	6
Total	101	13	6	7	117	32

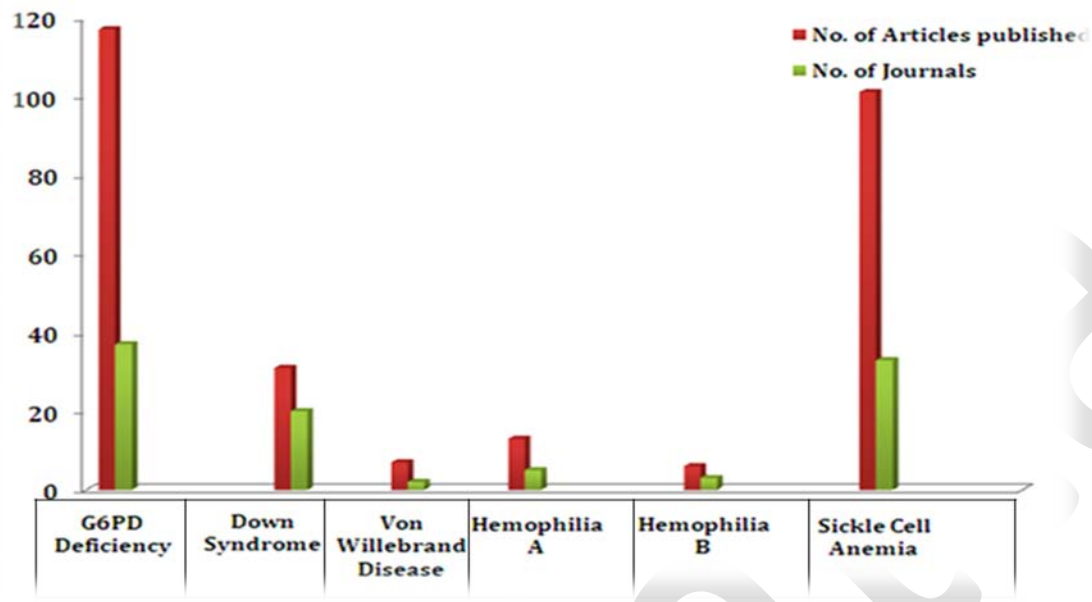
Most productive years of publications for different disorders were as follows-
SCA- 1987, HepA- 1990, HepB- --, vWD- ---, G6PD def- 1990, DS- 1990.

Table 4: Year- wise publications of articles on six genetic disorders published during 1991 – 2014 from India.

Year	Sickle cell anemia	Hemophilia 'A'	Hemophilia 'B'	von Willibrand disease	G6PD deficiency	Down syndrome
1991	6	1	1	0	3	4
1992	5	1	0	0	11	2
1993	9	4	2	2	5	2
1994	8	0	0	1	6	2
1995	5	1	0	1	5	1
1996	7	2	1	0	1	4
1997	10	2	2	0	6	7
1998	3	10	2	0	0	6
1999	5	8	0	0	2	1
2000	11	9	2	3	1	2
2001	5	15	8	0	6	4
2002	6	7	2	0	5	7
2003	3	14	4	5	7	9
2004	7	16	6	1	3	3
2005	12	12	1	10	6	8
2006	8	7	2	5	4	5
2007	9	17	6	2	8	11
2008	7	10	6	2	7	11
2009	8	12	5	3	7	11
2010	13	8	3	4	9	16
2011	14	12	6	5	5	13
2012	32	13	6	4	5	18
2013	25	12	5	7	2	23
2014	25	17	3	8	4	22
Total	**243**	**210**	**73**	**63**	**118**	**192**
Half Life Years	**18**	**16**	**17**	**18**	**13**	**19**

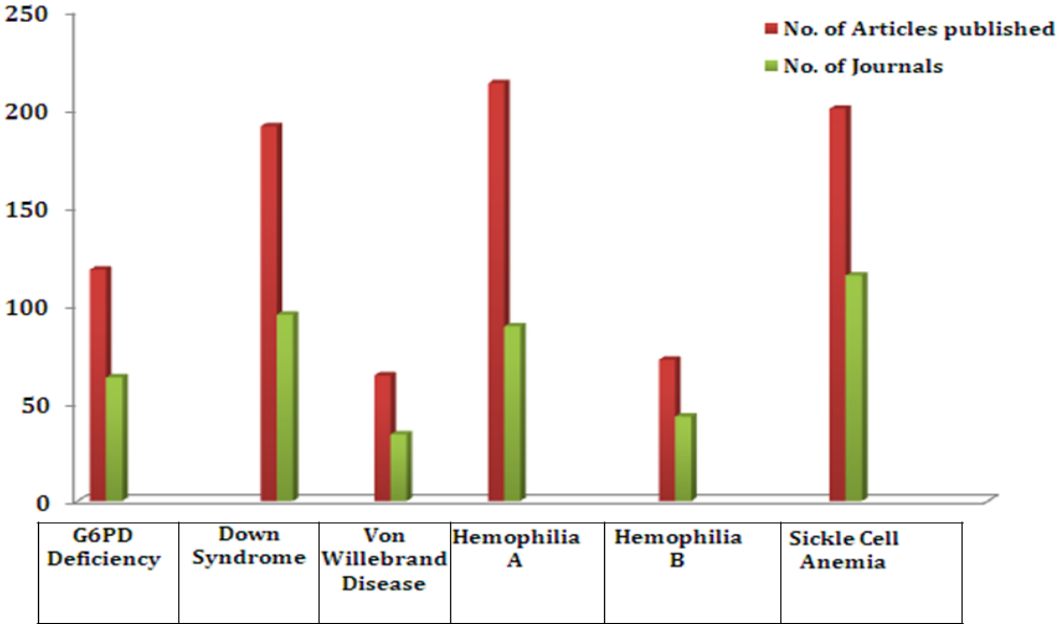
Most productive years of publications for different disorders were as follows-
SCA- 2013, 2014, HepA- 2007, 2014, HepB- 2001,
vWD- 2005, G6PD def- 1992, DS- 2013.

Figure 1: **Articles published up to 1990 from India on the six genetic disorders In various journals.**



Observation- Relatively small number of articles on von Willebrand disease, Hemophilia A and Hemophilia B have been published from India up to 1990 as compared to those published on remaining three disorders.

Figure 2: Articles published during 1991-2014 from India on six genetic disorders in various journals.



Observation- There is a considerable increase in number of articles published on vonWillebrand disease, Hemophilia A and Hemophilia B from India during 1991-2014 as compared to those published up to 1990 (fig 4.1).

Table 5: List of top five journals where maximum numbers of articles from India published on each genetic disorder up to 1990.

Genetic Disorder	Down syndrome	Sickle cell anemia	Hemophilia A	Hemophilia B	*von Willebrand disease	G6PD deficiency
Top Five Journals	Ind J Paed 05	JAPI 29	JAPI 09	JAPI 04	JAPI 06	JAPI 22
	Human Genetics 04	IJMR 11	IJMR 01	IJMR 01	Ind J Paed 01	IJMR 12
	IJMR 03	JIMA 07	Blood 01	Ind J Paed 01		IndPaed 11
	Lancet 03	IndPaed 06	BJCP 01			Ind J Patho & M 07
	IndPaed 02	Am J Haemat 05	Ind J Paed 01			Human Genetics 05
Total	**17**	**58**	**13**	**6**	**7**	**57**
Total No. Articles	**32**	**101**	**13**	**6**	**7**	**117**
No. of Independent Journals	**18**	**32**	**5**	**3**	**2**	**37**
% Representation of top 5 Journals	**27.78**	**15.63**	**100**	**100**	**100**	**13.51**
% Representation of Articles in top 5 Journals	**53.13**	**57.43**	**100**	**100**	**100**	**48.72**
% representation of Articles in first Journal	**15.53**	**28.71**	**69.23**	**66.67**	**85.71**	**18.8**
Articles/Journals	**1.78**	**3.16**	**2.6**	**2**	**3.5**	**3.16**

Ind J Patho& M - Indian Journal of Pathology and Microbiology, IndPaed – Indian PaedeatricsInd J Paed- Indian Journal of Paedeatrics, BJCP- British Journal of Clinical Practice, IMA-Journal of Indian Medical Association, IJMR – Indian Journal of Medical Research ,JAPI- Journal of Association of Physicians of India,
Am J Haemat – American Journal of Haematology.

*** There are no articles seen in PUBMED database during 1982 – 1990 on von Willebrand disease**

Table 6: List of top five journals where maximum numbers of articles from India are published on each genetic disorder during 1991 – 2014.

Genetic Disorder	Down syndrome	Sickle cell aanemia	Hemophilia A	Hemophilia B	von Willebrand disease	G6PD deficiency
Top Five Journals	Ind J Paed 26	JAPI 21	Haemophilia 63	Haemophillia 20	Ann Haemat 08	Ind J Paed 10
	IndPaed 14	Ind J Paaed 13	Sem In Thrombo Hem 08	Am J Haemat 03	Haemophilia 06	BCMD 06
	IJHG 09	Haemoglobin 13	CATH 08	EuroJ Haemat 03	Natl Med J Ind 04	JAPI 05
	JAPI 06	IJMR 07	J Thrombo Hem 06	Blood Co F I 02	Sem In Thrombo Hem 04	Ind J Mal 04
	PaedHaemoOnco 05	Ind J Patho& M 06	Ind J Paed 06	J Thrombo Hem 02	J Thrombo Hem 03	Anthro ANZ 04
Total	**60**	**60**	**91**	**30**	**25**	**29**
Total No. Articles	**192**	**243**	**210**	**73**	**63**	**118**
No. of Independent Journals	**95**	**115**	**85**	**44**	**34**	**62**
% Representation of top 5 Journals	**5.26**	**4.35**	**5.88**	**11.36**	**14.71**	**8.06**
% Representation of Articles in top 5 Journals	**31.25**	**24.69**	**43.33**	**41.10**	**39.68**	**24.58**
% representation of Articles in first Journal	**13.54**	**8.64**	**30.00**	**27.4**	**12.7**	**8.48**
Articles/Journals	**2.02**	**2.11**	**2.47**	**1.66**	**1.85**	**1.90**

Sem In Thrombo Hem – Seminars in Thrombosis and Haemotostasis , Ind J Patho& M - Indian Journal of Pathology and Microbiology, IndPaed – Indian Paedeatrics, BCMD – Blood Cells Molecules and Diseases J Thrombo Hem – Journal of Thrombosis and Haemostasis, Anthro ANZ- Anthropology ANZ, Ind J Mal- Indian Journal of Maleriology, Blood Co F I- Blood Coagulation and Fibrinolysis, Ind J Paed- Indian Journal of Paedeatrics, Am J Haemat – American Journal of Haematology, IJHG – Indian Journal of Human Genetics ,IJMR – Indian Journal of Medical Research,PaedHaemoOnco – PaediatricsHaematology and Oncology ,JAPI- Journal of Association of Physicians of India, CATH- Clinical Applications in Thrombosis and Haemostasis, Euro J Haemat – European Journal of Haematology,AnnHaemat – Annals of Haematology, Natl Med J Ind – National Medical Journal of India.

Conclusion

1. Indians cumulative publication output on the above mentioned six hereditary was negligible as compared to that from all over the world.
2. Half-life for all the disorders ranged between 13-19 years since 1991this clearly indicates that the number of publications was picked up during 2006-2014.
3. Comparatively less number of articles was published on coagulation disorders up to 1990.
4. During second time block (1991-2014) G6PD deficiency showed the reverse trend of publications, because the most productive year was 1992 and then slowly the number of publications was decreasing.
5. Availability of subject specific journals for publishing articles was one of the reasons for good growth for publications on coagulation disorders. Journals like "Hemophilia' "Journal of Thrombosis and Hemostasis" were established during last decade of 20th century.
6. Identification of most prominent journals would help the librarians to order these journals which would be useful for scientists who are working on these disorders.

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